Functional characterization of embryonic stem cell-derived endothelial cells.

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Public Summary:
Endothelial cells (EC) derived from embryonic stem cells (ESC) require additional functional characterization before they are used as a cell therapy. We explore several physiologically relevant functions of ESC-derived EC (ESC-EC), such as its capacity to produce nitric oxide (NO), regulate permeability, activate and express surface molecules for the recruitment of leukocytes in response to inflammatory stimuli, migrate and grow new blood vessels, lay down extracellular matrix, and take up low-density lipoproteins. We also examined the ESC-EC ability to upregulate NO in response to shear stress and downregulate NO in response to pro-inflammatory TNF-alpha activation. Functional responses of ESC-EC were compared with those of cultured mouse aortic ECs. The ESC-EC exhibit most aspects of functional endothelium, but interesting differences highlighted.

Scientific Abstract:
Endothelial cells (EC) derived from embryonic stem cells (ESC) require additional functional characterization before they are used as a cell therapy in order to enhance their potential for engraftment and proliferation. We explore several physiologically relevant functions of ESC-derived EC (ESC-EC), such as its capacity to produce nitric oxide (NO), regulate permeability, activate and express surface molecules for the recruitment of leukocytes in response to inflammatory stimuli, migrate and grow new blood vessels, lay down extracellular matrix, and take up low-density lipoproteins. We also examined the ESC-EC ability to upregulate NO in response to shear stress and downregulate NO in response to pro-inflammatory TNF-alpha activation. Functional responses of ESC-EC were compared with those of cultured mouse aortic ECs. The ESC-EC exhibit most aspects of functional endothelium, but interesting differences remain. The ESC-EC produced less NO on a per cell basis, but the same amount of NO if quantified based on the area of endothelial tissue. They also exhibit increased angiogenic sprouting and are more resistant to inflammatory signals. We further characterized the subphenotype of our ESC-EC and observed both venous and arterial markers on individual cells with a larger percentage of the cells exhibiting a venous phenotype. These data support the hypothesis that the developmental default pathway is toward a venous EC, and that refinement of methods for differentiation towards arterial EC is required to maintain a homogeneous population.